23/08/2016, The Netherlands: The European Society of Clinical Microbiology and Infectious Diseases (ESCMID) has just released new guidelines on best practice methods to diagnose *Clostridium difficile* infection (CDI). The latest document updates the original 2009 guidelines produced by the society, and includes recommendations concerning the use of new diagnostic technology such as nucleic acid amplification tests (NAAT).

“The new guidelines are intended for use among medical microbiologists, gastroenterologists, infectious disease specialists and infection control practitioners,” explains Professor Ed Kuijper of the Leiden University Medical Center, The Netherlands whose research group with Prof. Monique Crobach as first author have published the guidelines. “Our aim is to not only improve diagnosis of CDI, but also to standardise the diagnostic process across Europe to allow for improved surveillance of the disease.”

The study that underpins the new guidelines was initiated in June 2014 and comprises a meta-analysis of all relevant studies. Reports published after 2009 available in PubMed, Embase, Web of Science, Central and the Cochrane Library, together with pre-2009 studies included in the original meta-analysis were considered. The primary aim was to evaluate the diagnostic accuracy of commercially available lab tests in diagnosing CDI, and to make recommendations for standard testing algorithms.

In total 795 new studies were identified, of which 693 were excluded and 102 selected for review. Of these, a further 61 were excluded, leaving 41 studies to be taken forward and used to support the new guidelines. Reasons for exclusion included incorrect or inconsistent reference testing, incorrect or inconsistent index testing, incorrect sample storage and incomplete sample testing. A total of 43 studies were also considered from the original meta-analysis, of which 28 were excluded and 15 taken forward.

Various laboratory assays available from commercial suppliers were assessed for their ability to diagnose CDI accurately. A reference test, typically cell cytotoxicity neutralisation assay (CNNA) or toxigenic culture (TC) was used to investigate the accuracy of several tests that have emerged since 2009. These included enzyme immunoassays (EIA) that detect glutamate dehydrogenase or toxins A and B, and the new NAATs.

The guidelines rated both the strength of the recommendations from individual studies and the quality of the available evidence using a slightly modified version of the GRADE system and then recommendations were formulated using the Appraisal of Guidelines for Research and Evaluation (AGREE II) instrument.

Despite the development of new tests for CDI, the authors strongly recommend against the routine use of any single test, irrespective on the technology on which it is based.

The new guidelines also make recommendations on repeated testing for both positive and negative samples, as well as on the selection of samples to be tested.

The strongest recommendations based on the evidence from all studies in the meta-analysis are:

- Samples to be tested for CDI should not be limited to cases in which a physician has specifically recommended a test.
- A rectal swab can be used for testing by (toxigenic) culture, NAAT or GDH EIA in patients with apparent ileus (inactive bowel with no discernable bowel sounds)

- Single, standalone tests are not reliable and should not be used: a two-step algorithm is necessary.

This two-step algorithm involves a combination of fast assays with follow up tests:

- **Route one** – the two-stage procedure should begin with either an NAAT or GDH EIA test. Negative tests should be treated as CDI negative, while positive tests should be followed up with a toxin A/B EIA test to confirm the result.

- **Route two** – the two-stage procedure should begin with both the GDH EIA test and the toxin A/B EIA test. If both are positive, CDI is likely to be present. If both are negative, CDI is unlikely to be present, however if GDH is positive and toxin A/B is negative, then the tests may optionally be followed up with an NAAT or TC test.

In endemic situations, repeat testing is not recommended after a positive result has been obtained but is advised after an initial negative sample from a patient with persistent high clinical suspicion.

The updated guidelines were published in ESCMID's journal *Clinical Microbiology and Infection* as a supplement and are freely available here.

**ENDS**

**Notes to editors**

Several commercial tests for diagnosing CDI have been released and marketed since 2009 but their accuracy has never been studied in comparison with previously validated assays.

CDI is a leading cause of diarrhoea contracted within healthcare environments in the developed world. Disease is due to strains of *Clostridium difficile* that produce either toxin A or toxin B. Diagnosing the presence of these strains needs to be achieved quickly and accurately.

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